Scientists identify potential drug target for inflammatory diseases including cancers

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A*STAR scientists have identified the enzyme, telomerase, as a cause of chronic inflammation in human cancers. Chronic inflammation is now recognized as a key underlying cause for the development of many human cancers, autoimmune disorders, neurodegenerative diseases, and metabolic diseases such as diabetes. This enzyme, which is known to be responsible for providing cancer cells the endless ability to divide, is now found to also jumpstart and maintain chronic inflammation in cancers.

In identifying this enzyme, inflammation can be prevented or reduced, and the common ailments can be alleviated. This discovery has considerable impact on healthcare because developing drugs to target telomerase can greatly reduce healthcare costs.

Currently, the annual costs and expenses associated with cancer and metabolic diseases such as diabetes amount to about $132 billion in the US alone. Although many safe and effective anti-inflammatory drugs such as aspirin are currently available on the market, these drugs sometimes have side effects because blocking inflammation is typically detrimental to normal physiology. Hence there exists a need for the development of cost-effective drugs that are targeted, so as to minimize side effects. The research findings were published on Nov. 18, 2012, in the prestigious scientific journal, Nature Cell Biology.

The team identified that telomerase directly regulates the production of inflammatory molecules that are expressed by NF-kB, a known master regulator of chronic inflammation. These molecules are critical for

inflammation and cancer progression. By inhibiting telomerase activity in primary cancer cells obtained from patient samples, the scientists found that levels of IL-6, an inflammatory molecule known to be a key driver of human cancers, was reduced in expression as well. This is an important breakthrough that shows how targeting telomerase with drugs could potentially reduce inflammation, and hence get rid of cancer cells.

Dr Tergaonkar said, "These findings provide a unifying explanation for a decade worth of observations from leading laboratories in the field which show that chronic inflammation and telomerase hyperactivity co-exist in over 90 percent of human cancers. What we show that these two activities are actually interdependent. They also may lead to potentially novel drugs that will target a range of human ailments with inflammation as an underlying cause, which range from arthritis to cancer."

Prof Hong Wan Jin, Executive Director of IMCB, said, "The discovery speaks for the exceptional power of identifying novel mechanisms that have translational potential, through close collaborations among scientists in different A*STAR institutes, as well as to bring together both basic and clinical research scientists in Singapore. I am confident that we can expect more discoveries like this from Dr Tergaonkar's team."

More information: Ghosh, A. et al., Telomerase directly regulates NF-kB-dependent transcription, *Nature Cell Biology*. November 18, 2012.

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